General

Guideline Title

Current status in non-invasive prenatal detection of Down syndrome, trisomy 18, and trisomy 13 using cell-free DNA in maternal plasma.

Bibliographic Source(s)

Langlois S, Brock JA, Genetics Committee. Current status in non-invasive prenatal detection of down syndrome, trisomy 18, and trisomy 13 using cell-free DNA in maternal plasma. J Obstet Gynaecol Can. 2013 Feb;35(2):177-81. [21 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The quality of evidence (I-III) and classification of recommendations (A-E, L) are defined at the end of the "Major Recommendations" field.

1. Non-invasive prenatal testing using massive parallel sequencing of cell-free fetal deoxyribonucleic acid (cffDNA) to test for trisomies 21, 18, and 13 should be an option available to women at increased risk in lieu of amniocentesis. Pretest counselling of these women should include a discussion of the limitations of non-invasive prenatal testing. (II-2A)
2. No irrevocable obstetrical decision should be made in pregnancies with a positive non-invasive prenatal testing result without confirmatory invasive diagnostic testing. (II-2A)
3. Although testing of cffDNA in maternal plasma appears very promising as a screening test for Down syndrome and other trisomies, studies in average-risk pregnancies and a significant reduction in the cost of the technology are needed before this can replace the current maternal screening approach using biochemical serum markers with or without fetal nuchal translucency ultrasound. (III-A)

Definitions:

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments

(such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

†Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Fetal chromosomal abnormalities, including:

- Down syndrome
- Trisomy 18
- Trisomy 13

Guideline Category

Counseling

Diagnosis

Screening

Clinical Specialty

Family Practice

Medical Genetics

Obstetrics and Gynecology

Pediatrics

Intended Users

Clinical Laboratory Personnel

Nurses

Physicians

Guideline Objective(s)

To provide a review of published studies on the use of cell-free fetal deoxyribonucleic acid (cffDNA) in maternal plasma for the non-invasive diagnosis of Down syndrome, trisomy 18, and trisomy 13

Target Population

Women with pregnancies at high risk for chromosomal abnormalities

Interventions and Practices Considered

1. Non-invasive prenatal testing using cell-free fetal deoxyribonucleic acid (cffDNA)
2. Confirmatory invasive diagnostic testing
3. Pretest counseling

Major Outcomes Considered

- Detection rate
- False positive rate
- Failure rate

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

PubMed was searched for articles published between 2006 and October 2012, using appropriate key words (e.g., non-invasive prenatal diagnosis, Down syndrome, cell-free fetal DNA, aneuploidy screening). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. Searches were updated on a regular basis and incorporated in the guideline to October 31, 2012. Grey (unpublished) literature was identified through searching the Web sites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

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II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The studies reviewed were classified according to criteria described by the Canadian Task Force on Preventive Health Care, and the recommendations for practice were ranked according this classification.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

†Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This committee opinion has been prepared by the Genetics Committee and approved by the Executive of the Society of Obstetricians and Gynaecologists of Canada.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The development of new screening methods to detect Down syndrome through testing of cell-free fetal deoxyribonucleic acid (cffDNA) in maternal plasma offers promising opportunities to improve prenatal screening.

Potential Harms

- Cell-free fetal deoxyribonucleic acid (cffDNA) testing has a higher rate of false-positive results than current diagnostic tests based on cytogenetic analysis of amniocytes or chorionic villi (see Tables 2 and 3 in the original guideline document for more information regarding false-positive rate).
- Some women will have a cffDNA positive result and not carry a fetus with Down syndrome, trisomy 18, or trisomy 13 (false-positive).
- cffDNA testing fails to provide a result in a small percentage of women.

Qualifying Statements

Qualifying Statements

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

Implementation of the Guideline

Description of Implementation Strategy

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Feb

Guideline Developer(s)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

Source(s) of Funding

Society of Obstetricians and Gynaecologists of Canada

Guideline Committee

Genetics Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Disclosure statements have been received from all members of the committee.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada (SOGC) Web site. Also available in French from the SOGC Web site.

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

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